FILE CAPLUS 3/14/07

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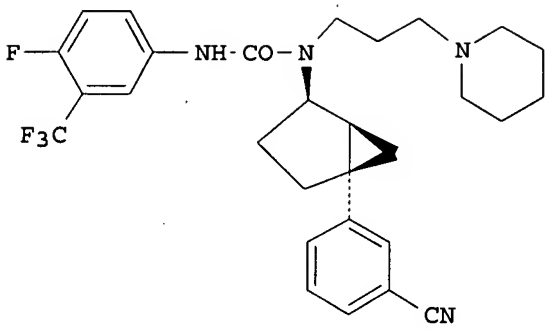
L5 ANSWER 1 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1245016 CAPLUS
DOCUMENT NUMBER: 146:92471
TITLE: Melanin-concentrating hormone MCH1 receptor antagonists A potential new approach to the treatment of depression and anxiety disorders
AUTHOR(S): Shimazaki, Toshiharu; Yoshimizu, Takao; Chaki, Shigeyuki
CORPORATE SOURCE: Medicinal Pharmacology Laboratory, Medicinal Research Laboratories, Taisho Pharmaceutical Co. Ltd, Saitama, Japan
SOURCE: CNS Drugs (2006), 20(10), 801-811
CODEN: CNDREF; ISSN: 1172-7047
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Melanin-concentrating hormone (MCH) is a cyclic 19-amino-acid neuropeptide that has been considered to play a key role in the regulation of feeding and energy homeostasis. To date, two receptor subtypes for MCH (designated MCH1 and MCH2) have been identified; the MCH1 receptor has been proposed to mediate the physiol. functions of MCH in rodents. In addition to the crucial roles of MCH in feeding behavior, anatomical and neurochem. studies suggest that the MCH/MCH1 system is involved in the regulation of emotion and stress responses. This assumption has been supported by a recent series of neurochem. and behavioral studies. Indeed, several lines of evidence show that MCH activates stress responses and induces depressive- and anxiety-like behaviors, while the blockade of MCH1 receptors results in antidepressant and anxiolytic effects in various rodent models. Moreover, MCH may decrease reward activity while increasing hypothalamus-pituitary adrenal axis activity, both of which may underlie the neurochem. mechanisms of the depression and anxiety-like effects induced by MCH. The effects of MCH1 receptor antagonists in animal models, together with their rapid onset of effect and lack of adverse CNS effects, suggest that they deserve further investigation as potential new treatments for depression and anxiety disorders.
REFERENCE COUNT: 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:608602 CAPLUS
DOCUMENT NUMBER: 145:83317
TITLE: Preparation of N-benzothiazolyl(or benzoxazolyl) amides as novel MCH receptor antagonists for treating and preventing symptoms associated with obesity and related diseases
INVENTOR(S): Beck, James Peter; Wakefield, Brian David; Cordier, Frederic Laurent; Dominguez-Manzanares, Esteban; Gardinier, Kevin Matthew; Greenen, Peter Michael; Savin, Kenneth Allen
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE



I

AB The present invention discloses N-aryl-N'-arylcycloalkylureas (Ar2N(R2)C(:X)N(YR1)(ZAr1); I; variables defined below; e.g. N'-(3-trifluoro-4-fluorophenyl)-N-[trans-4-(3-cyanophenyl)-4-hydroxycyclohexyl]-N-[2-(1-pyrrolidinyl)ethyl]urea hydrochloride), which are novel antagonists for melanin-concentrating hormone (MCH), as well as methods for preparing such compds. In another embodiment, the invention discloses pharmaceutical compns. comprising such MCH antagonists as well as methods of using them to treat obesity, metabolic disorders, eating disorders such as hyperphagia, and diabetes. For I: Ar1 is aryl, heteroaryl, (R7)p-substituted aryl or (R7)p-substituted heteroaryl (p = 1-3; each R7 = alkyl, cycloalkyl, halo, -CN, alkoxy, -CF3, -OCF3, pyrazolyl, etc.). Ar2 is aryl, heteroaryl, (R7)p-substituted aryl or (R7)p-substituted heteroaryl (p = 1-3; each R7 = alkyl, cycloalkyl, halo, -CN, alkoxy, -CF3, -OCF3, pyrazolyl, etc.); X is O, S or N-(CN); Y is a single bond or alkylene; Z is a C4-C8 cycloalkylene or C4-C8 heterocycloalkylene; or R1 is -N(R3)2, -N(H)C(O)alkyleneN(R3)2, -C(O)N(H)alkyleneN(R3)2, -C(O)N(alkyl)alkyleneN(R3)2, -alkyleneC(H)(OH)alkyleneN(R3)2, -N(alkyl)alkyleneN(R3)2, -N(H)alkyleneC(O)R5, -N(alkyl)alkyleneN(alkyl)SO2R5 or -N(alkyl)alkyleneC(O)N(R3)2; R2 = H, alkyl; addnl. details are given in the claims. Although the methods of preparation are not claimed, many example prepns. and characterization data for hundreds of I are included. Ki values for binding of many I to the MCH receptor are tabulated; they range from 1 to 600 nM, e.g. 1.6 nM for II.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 26 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:423613 CAPLUS
DOCUMENT NUMBER: 139:332099
TITLE: Does the melanin-concentrating hormone antagonist SNAP-7941 deserve 3As?
AUTHOR(S): Doggrell, Sheila A.
CORPORATE SOURCE: School of Biomedical Sciences, The University of Queensland, QLD 4072, Australia
SOURCE: Expert Opinion on Investigational Drugs (2003), 12(6), 1035-1038
CODEN: EOIDER; ISSN: 1354-3784
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Melanin-concentrating hormone (MCH) is orexigenic (stimulates food intake). Two receptors for MCH have been identified in humans, MCH1-R and MCH2-R. SNAP-7941 is a small mol. MCH1-R antagonist. SNAP-7941 inhibits MCH-induced food intake in rats. SNAP-7941 alone reduced weight gain in young growing rats and in mature rats fed a high-fat diet. Preliminary testing with SNAP7941 in animal models of depression and anxiety

shows it has antidepressant and anxiolytic effects. SNAP7941 should undergo further development as an anorectic, antidepressant and anxiolytic.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 27 OF 30 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:335085 CAPLUS
DOCUMENT NUMBER: 138:353842
TITLE: Preparation of quinoline derivatives as melanin-concentrating hormone antagonists
INVENTOR(S): Ishihara, Yuji; Kamata, Makoto; Takekawa, Shiro; Suzuki, Nobuhiro; Kato, Koki
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 346 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003035624	A1	20030501	WO 2002-JP11045	20021024
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2464981	A1	20030501	CA 2002-2464981	20021024
JP 2004059567	A	20040226	JP 2002-309175	20021024
EP 1447402	A1	20040818	EP 2002-777944	20021024
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002013521	A	20041019	BR 2002-13521	20021024
CN 1585751	A	20050223	CN 2002-826244	20021024
US 2005209213	A1	20050922	US 2004-493427	20040423
US 7183415	B2	20070227		
NO 2004002121	A	20040624	NO 2004-2121	20040524
IN 2004KN00685	A	20060505	IN 2004-KN685	20040524

PRIORITY APPLN. INFO.:
JP 2001-327924 A 20011025
JP 2002-163239 A 20020604
WO 2002-JP11045 W 20021024

OTHER SOURCE(S): MARPAT 138:353842
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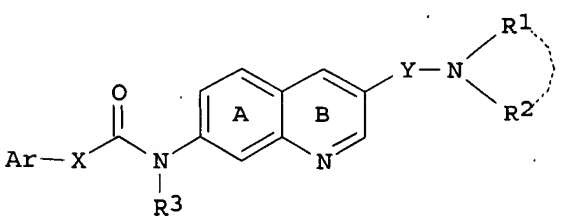

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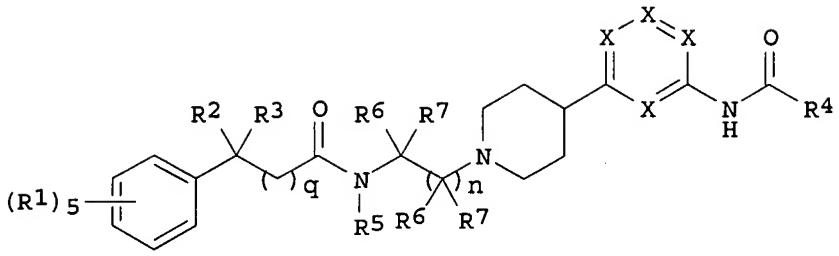

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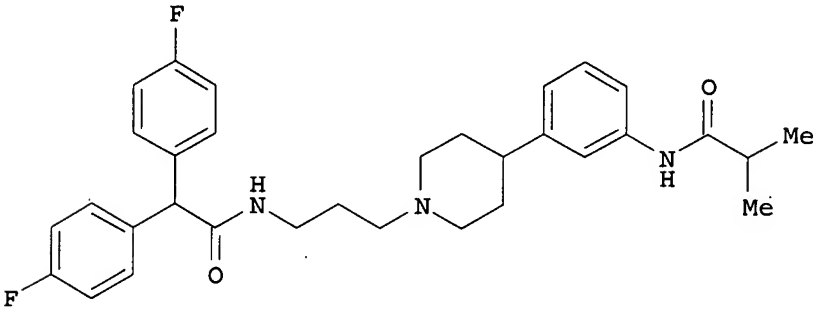


II

AB Title compds. I [wherein R1 = independently H, halo, CN, NO2, (cyclo)alkyl, (cyclo)alkenyl, (hetero)aryl, amino, acyl, carbamoyl, etc.; R2, R3 = independently H, halo, CN, NH2, (un)substituted alkyl, (hetero)aryl; R4 = (cyclo)alkyl, amino, etc.; R5 = independently H, (un)substituted (hetero)aryl, alkyl; R6 = independently H, alkyl; R7 = independently H, alkyl, phenyl(alkyl); n = 1-5; q = 0-2; X = independently CR1, N, provided that if one X = N, then the remaining X = CR1; or pharmaceutically acceptable salts thereof] were prepared as selective antagonists for melanin-concentrating hormone-1 (MCH1) receptors. For example, amidation of bis(4-fluorophenyl)acetic acid with N-[3-[1-(3-aminopropyl)-4-piperidinyl]phenyl]-2-methylpropanamide gave II. The latter showed binding affinity (Ki = 1.3 nM) in a radioligand binding assay using cloned rat MCH1 and produced an increase in bladder capacity in rats relative to baseline capacity in a continuous slow transvesicular infusion model assay. Thus, I and pharmaceutical composition comprising I are useful for the treatment of obesity, depression, anxiety, and other affective, urinary, or eating disorders.

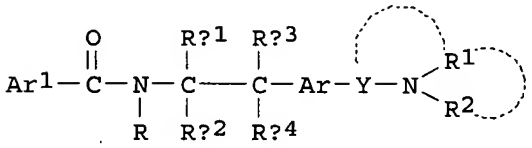
L8 ANSWER 13 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:696336 CAPLUS
DOCUMENT NUMBER: 141:207231
TITLE: Preparation of N-phenethylpiperidine-1-carboxamide, N-phenethylbenzamides, and N-phenethylbiphenyl-4-carboxamide derivatives as melanin-concentrating hormone antagonists
INVENTOR(S): Ishihara, Yuji; Kamata, Makoto; Takekawa, Shiro
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 227 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004072018	A1	20040826	WO 2004-JP1467	20040212

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

JP 2004262931	A	20040924	JP 2004-34598		20040212
EP 1593667	A1	20051109	EP 2004-710515		20040212
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
US 2006128690	A1	20060615	US 2005-545120		20050810
PRIORITY APPLN. INFO.:			JP 2003-34010	A	20030212
			WO 2004-JP1467	W	20040212

OTHER SOURCE(S): MARPAT 141:207231
GI



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AB Amine compds. represented by the formula (I) or salts thereof [Ar1 = (un)substituted cyclic group; R = H, C1-6 alkyl, halo-C1-6 alkyl, each (un)substituted Ph or pyridyl; Ra1-Ra4 = H, C1-6 alkyl, halo-C1-6 alkyl, halo, cyano, C1-6 alkoxy-, halo-C1-6 alkoxy, C1-6 alkylthio, halo-C1-6 alkylthio, NH2, mono- or di(C1-6 alkyl)amino, CHO, C1-6 alkylcarbonyl, halo-C1-6 alkylcarbonyl, C1-6 alkylsulfonyl, halo-C1-6 alkylsulfonyl, each (un)substituted pyridyl or Ph; Ar = (un)substituted mono cyclic aromatic ring; Y = alkylene or haloalkylene; R1 , R2 = H, C1-6 alkyl; or NR1R2 together forms (un)substituted N-containing heterocyclic ring; or NR1 and Y together forms (un)substituted N-containing heterocyclic ring and R2 = H or C1-6 alkyl; provided that when NR1R2 together forms N- containing heterocyclic ring or R = C1-4 alkyl, Ar1 = (un)substituted cyclic group] are prepared These compds. have antagonistic activity against melanin-concentrating hormone (MCH) and are useful as preventives/therapeutic agents for obesity, depression, or anxiety, or as antifeeding agents (appetite depressants). For example, N-[2-[4-[1-(1-azepanyl)ethyl]phenyl]ethyl]-4'-chloro-1,1'-biphenyl-4-carboxamide showed IC50 of 3 nM for inhibiting the binding of [36S]-guanosine 5'-(γ-thio)triphosphate to CHO cells expressing human SLC-1 receptor (MCH1). A tablet formulation containing 4'-chloro-N-[2-[4-(1-pyrrolidinylmethyl)phenyl]propyl]-1,1'-biphenyl-4-carboxamide was prepared

L8 ANSWER 14 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2004:390211 CAPLUS
DOCUMENT NUMBER:	140:406638
TITLE:	Preparation of arylamides as melanin concentrating hormone (MCH) receptor antagonists.
INVENTOR(S):	Stenkamp, Dirk; Mueller, Stephan Georg; Roth, Gerald Juergen; Lustenberger, Philipp; Rudolf, Klaus; Lehmann-Lintz, Thorsten; Arndt, Kirsten; Lotz, Ralf R. H.; Lenter, Martin; Wieland, Heike-Andrea
PATENT ASSIGNEE(S):	Boehringer Ingelheim Pharma GmbH & Co. Kg, Germany; et al.
SOURCE:	PCT Int. Appl., 276 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent

LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039764	A1	20040513	WO 2003-EP11933	20031028
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10250743	A1	20040519	DE 2002-10250743	20021031
CA 2504207	A1	20040513	CA 2003-2504207	20031028
AU 2003285306	A1	20040525	AU 2003-285306	20031028
EP 1558567	A1	20050803	EP 2003-778292	20031028
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003015797	A	20050913	BR 2003-15797	20031028
CN 1708476	A	20051214	CN 2003-80102236	20031028
JP 2006504761	T	20060209	JP 2004-547576	20031028
US 2004152742	A1	20040805	US 2003-699089	20031031
NO 2005000745	A	20050523	NO 2005-745	20050211
PRIORITY APPLN. INFO.:			DE 2002-10250743 A	20021031
			US 2003-456482P P	20030321
			WO 2003-EP11933 W	20031028

OTHER SOURCE(S): MARPAT 140:406638

AB R1R2NXYZNR3COWABb [R1, R2 = H, (substituted) alkyl, cycloalkyl, heterocyclyl, Ph, pyridyl; R1R2 = alkylene optionally interrupted by CH:N, CH:CH, O, S, SO, SO2, CO, imino, etc.; R3 = H, alkyl, cycloalkyl, cycloalkylalkyl; X = alkylene optionally interrupted by CH:CH, C.tplbond.C, O, S, SO, SO2, CO, imino; W = CR6aR6bO, CR7a:CR7c, etc.; Z = bond, (fused) (alkyl-substituted) alkylene; Y, A, B = Cy; b = 0, 1; Cy = (substituted) (unsatd.) carbocyclyl, Ph, (aromatic) heterocyclyl; R6a, R6b = H, alkyl, CF3; R7a, R7c = H, F, Cl, alkyl, CF3; with provisos and specific exceptions], were prepared for treatment of obesity, diabetes, heart failure, arteriosclerosis, hypertension, arthritis, mastocytosis, depression, anxiety, etc. Thus, Me aminoacetate hydrochloride, Et3N, and N-[3-chloro-4-(2-oxoethoxy)phenyl]-2-(2,4-dichlorophenoxy)acetamide in CH2Cl2/THF were treated with NaBH(OAc)3 followed by stirring for 3 h to give 78% Me [2-[2-chloro-4-[2-(2,4-dichlorophenoxy)acetylamino]phenoxy]ethylamino]acetate. Tested title compds. bound to MCH-1 receptors with IC50 = 17-41 nM.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 23 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:198178 CAPLUS
DOCUMENT NUMBER: 140:235748
TITLE: Preparation of arylquinoazolinones and related compounds as melanin concentrating hormone (MCH) antagonists.
INVENTOR(S): Stenkamp, Dirk; Lehmann-Lintz, Thorsten; Mueller, Stephan; Rudolf, Klaus; Lustenberger, Phillip; Arndt, Kirsten; Lotz, Ralf; Wieland, Heike; Lenter, Martin
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Novo Nordisk A/S
SOURCE: Ger. Offen., 132 pp.

L9 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:444897 CAPLUS
DOCUMENT NUMBER: 145:201849
TITLE: Development of a time-resolved fluorometric assay for the high throughput screening of melanin concentrating hormone receptor antagonists
AUTHOR(S): Lee, Sunghou; Kim, Gun-Do; Park, Woo-Kyu; Cho, Heeyeong; Lee, Byung Ho; Yoo, Sung-eun; Kong, Jae Yang
CORPORATE SOURCE: Department of Biotechnology and Informatics, College of Engineering, Sangmyung University, Cheonan, 330-720, S. Korea
SOURCE: Journal of Pharmacological and Toxicological Methods (2006), 53(3), 242-247
CODEN: JPTMEZ; ISSN: 1056-8719
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Melanin concentrating hormone is an orexigenic hypothalamic neuropeptide, which plays an important role in the complex regulation of energy balance and body weight mediated by the melanin concentrating hormone receptor subtype 1 (MCH1).
Compelling pharmacol. evidence implicating MCH1 signaling in the regulation of food intake and energy expenditure has generated a great deal of interest by pharmaceutical companies as MCH1 antagonists may have potential therapeutic benefit in the treatment of obesity and metabolic syndrome. Although radioligand receptor binding assay has been one of the most powerful tools for receptor research and drug discovery, the limitations of radioisotopes and the problems related to safety and waste disposal limits their application in high throughput screening and has led to a growing interest in alternative, nonradioactive technologies. To develop a sensitive and reproducible assay system for MCH1, the time-resolved fluorescence (TRF) receptor binding assay with AcroWell filter plates was tested and validated. Comparing to the radioligand receptor binding assay for MCH1, the TRF assay presented higher Z/Z' factors with the lower signal-to-noise ratio. The known high-affinity MCH1 receptor antagonist, SNAP-7941, exhibited an IC50 value of 1.66±0.10 nM that is very similar to the IC50 value of MCH in a radioligand binding assay with an excellent correlation coefficient (0.9884). These results suggest that our TRF receptor binding assay for MCH1 can achieve the desired sensitivity and reproducibility to replace the radioligand receptor assay in a fluorometric system that can be developed for high throughput screening.
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:315598 CAPLUS
DOCUMENT NUMBER: 144:363300
TITLE: Effects of a selective melanin-concentrating hormone 1 receptor antagonist on food intake and energy homeostasis in diet-induced obese mice
AUTHOR(S): Kowalski, Timothy J.; Spar, Brian D.; Weig, Blair; Farley, Constance; Cook, John; Ghibaudi, Lorraine; Fried, Steve; O'Neill, Kim; Del Vecchio, Robert A.; McBriar, Mark; Guzik, Henry; Clader, John; Hawes, Brian E.; Hwa, Joyce
CORPORATE SOURCE: Department of CV/Metabolic Diseases, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA
SOURCE: European Journal of Pharmacology (2006), 535(1-3), 182-191
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Melanin concentrating hormone (MCH) is a cyclic neuropeptide expressed in the lateral hypothalamus that plays an important role in energy homeostasis. To investigate the pharmacol. consequences of inhibiting MCH signaling in murine obesity models, we examined the effect of acute and chronic administration of a selective MCH1 receptor antagonist (SCH-A) in diet-induced obese (DIO) and Lep ob/ob mice. Oral administration of SCH-A for 5 consecutive days (30 mg/kg q.d.) produced hypophagia, a loss of body weight and adiposity, and decreased plasma leptin levels in DIO mice, and hypophagia and reduced weight gain in Lep ob/ob mice. Chronic administration of SCH-A to DIO mice decreased food intake, body weight and adiposity, and plasma leptin and free fatty acids. These effects were accompanied by increases in several hypothalamic neuropeptides. Acute administration of SCH-A (30 mg/kg) prevented the decrease in energy expenditure associated with food restriction. These results indicate that MCH1 receptor antagonists may be effective in the treatment of obesity
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REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:304660 CAPLUS
DOCUMENT NUMBER: 142:373570
TITLE: Preparation of tetrahydronaphthalene derivatives as melanin concentrating hormone antagonists
INVENTOR(S): Hu, Xiufeng Eric
PATENT ASSIGNEE(S): The Procter & Gamble Company, USA
SOURCE: U.S. Pat. Appl. Publ., 28 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005075324	A1	20050407	US 2004-949841	20040924
AU 2004278352	A1	20050414	AU 2004-278352	20040924
CA 2540826	A1	20050414	CA 2004-2540826	20040924
WO 2005033063	A2	20050414	WO 2004-US31631	20040924
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EP 1667958	A2	20060614	EP 2004-789086	20040924
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BR 2004015051	A	20061128	BR 2004-15051	20040924
NO 2006001953	A	20060613	NO 2006-1953	20060502
US 2006247239	A1	20061102	US 2006-473478	20060623

PRIORITY APPLN. INFO.:	US 2003-507773P	P	20031001
	US 2004-536640P	P	20040115
	US 2004-949841	A2	20040924
	WO 2004-US31631	W	20040924

OTHER SOURCE(S): CASREACT 142:373570; MARPAT 142:373570

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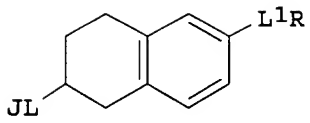

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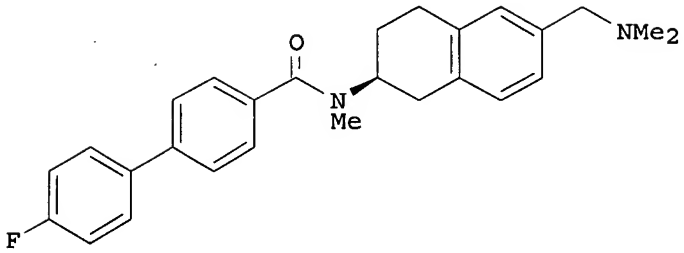

II

AB The present invention relates to compds. I [R = NR1R2; R1, R2 = H, OH, (un)substituted, (un)branched, cyclic C1-8-alkyl, C2-8-alkenyl; NR1R2 = (un)substituted heterocyclic, heteroaryl 3- to 15-membered ring; L, L1 = linking groups, (Z)j(CR3aR3b)m(Z1)j(R4aR4b)n(Z2)j; Z, Z1, Z2 = NR5, O, SO2, NR5SO2, SO2NR5; j = 0, 1; R5 = H, linear, branched or cyclic C1-4-alkyl; R3a, R3b, R4a, R4b = H, OH, halogen, linear, branched or cyclic C1-4-alkyl, C1-4-haloalkyl, C1-4-alkoxy; CR3aR3b, CR4aR4b = C:X; X = O, S, NR5; m, n = 0 - 5; optionally, when m, n = 2 then R3bR3b, R4bR4b = bond; J = AB, especially, C6H4(C6H4Ra)-4; A, B = carbocyclic, aryl, heterocyclic, heteroaryl (with the proviso that at least one of A and B = aryl, heteroaryl); Ra = F, Cl, NO2, CN, OH, NH2, NMe2, OMe, NC(:O)Me, CO2R7, CF3, linear, branched or cyclic C1-4-alkyl; R7 = H, linear, branched or cyclic C1-10-alkyl], their enantiomers, stereoisomers and their pharmaceutically acceptable salts, capable of serving as moderators of human and mammalian appetite and as such provides a means for reducing body mass. Thus, 4'-fluoro-1,1'-biphenyl-4-carboxylic acid N-[(S)-6-(dimethylamino)methyl-1,2,3,4-tetrahydronaphthalen-2-yl]-N-methylamide (II) was prepared from 6-bromo-1,2,3,4-tetrahydronaphthalen-2-amine via reductive ammoniation with NH4OH in MeOH containing NaCNBH3, amidation of 4'-fluoro-1,1'-biphenyl-4-carboxylic acid in DMF containing EDCI, HOBT and Et3N, cyanation with Zn(CN)2 in NMP containing Et3Zn and catalytic Pd(OAc)2/P(C6H4Me-4)3, methylation with MeI in DMF containing NaH, reduction over Raney Ni in DMF containing NH4OH, dimethylation with HCHO in DMF containing NaBH(OAc)3 and isolation of the S enantiomer. The compds. of the present invention are selective against melanin concentrating hormone and do not have the pernicious side effects resulting from compds. which interact with other appetite related brain receptors. The melanin concentrating hormone antagonistic activity of II was determined [IC50 = 60 nM vs. MCH-1 receptor; IC50 = 100,000 nM vs. 5-HT2C receptor].

L9 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:780358 CAPLUS

DOCUMENT NUMBER: 141:295863
TITLE: Preparation of N-(piperidinylalkyl)benzenealkanamides as selective MCH1 receptor antagonists for treatment of obesity and other conditions
INVENTOR(S): Marzabadi, Mohammad R.; Wetzel, John M.; Chen, Chien-An; Jiang, Yu; Lu, Kai
PATENT ASSIGNEE(S): Synaptic Pharmaceutical Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 87 pp., Cont.-in-part of U.S. Pat. Appl. 2004 73,036.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004186103	A1	20040923	US 2004-753057	20040106
US 2006084649	A9	20060420		
WO 2003004027	A1	20030116	WO 2002-US21063	20020703
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
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US 6727264	B1	20040427	US 2002-188434	20020703
US 2004073036	A1	20040415	US 2003-345063	20030114
~~US 2006041139~~	A9	20060223		
US 7105544	B2	20060912		
~~AU 2004206794~~	A1	20040805	AU 2004-206794	20040106
CA 2509456	A1	20040805	CA 2004-2509456	20040106
WO 2004064764	A2	20040805	WO 2004-US175	20040106
WO 2004064764	A3	20050113		
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EP 1590326	A2	20051102	EP 2004-700366	20040106
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2004006725	A	20051220	BR 2004-6725	20040106
CN 1735595	A	20060215	CN 2004-80002080	20040106
JP 2006515618	T	20060601	JP 2006-500796	20040106
NO 2005003838	A	20050815	NO 2005-3838	20050815

PRIORITY APPLN. INFO.:		
US 2001-303091P	P	20010705
US 2002-346997P	P	20020109
US 2002-188434	A2	20020703
WO 2002-US21063	A2	20020703
US 2003-345063	A2	20030114
US 2001-899794	A	20010705
US 2002-42582	A	20020109
WO 2004-US175	W	20040106

OTHER SOURCE(S): MARPAT 141:295863
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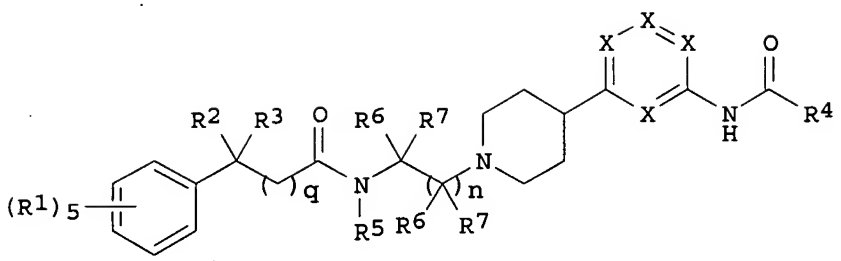

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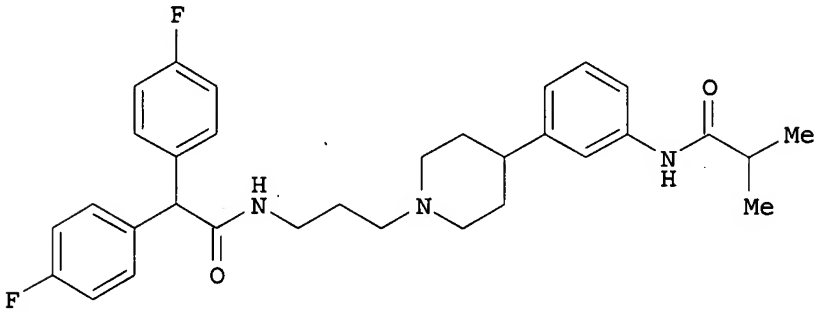

II

AB Title compds. I [wherein R1 = independently H, halo, CN, NO2, (cyclo)alkyl, (cyclo)alkenyl, (hetero)aryl, amino, acyl, carbamoyl, etc.; R2, R3 = independently H, halo, CN, NH2, (un)substituted alkyl, (hetero)aryl; R4 = (cyclo)alkyl, amino, etc.; R5 = independently H, (un)substituted (hetero)aryl, alkyl; R6 = independently H, alkyl; R7 = independently H, alkyl, phenyl(alkyl); n = 1-5; q = 0-2; X = independently CR1, N, provided that if one X = N, then the remaining X = CR1; or pharmaceutically acceptable salts thereof] were prepared as selective antagonists for melanin-concentrating hormone-1 (MCH1) receptors. For example, amidation of bis(4-fluorophenyl)acetic acid with N-[3-[1-(3-aminopropyl)-4-piperidinyl]phenyl]-2-methylpropanamide gave II. The latter showed binding affinity (Ki = 1.3 nM) in a radioligand binding assay using cloned rat MCH1 and produced an increase in bladder capacity in rats relative to baseline capacity in a continuous slow transvesicular infusion model assay. Thus, I and pharmaceutical composition comprising I are useful for the treatment of obesity, depression, anxiety, and other affective, urinary, or eating disorders.

L9 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:690505 CAPLUS
DOCUMENT NUMBER: 141:235457
TITLE: Therapeutic potential of melanin-concentrating hormone-1 receptor antagonists for the treatment of obesity
AUTHOR(S): Kowalski, Timothy J.; McBriar, Mark D.
CORPORATE SOURCE: Departments of Cardiovascular/Metabolic Disease Research, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA
SOURCE: Expert Opinion on Investigational Drugs (2004), 13(9), 1113-1122
CODEN: EOIDER; ISSN: 1354-3784
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The compelling genetic and pharmacol. evidence implicating melanin-concentrating hormone-1 receptor (MCH-1R) signaling in the regulation of

food intake and energy expenditure has generated a great deal of interest by pharmaceutical companies for the discovery of MCH-1R antagonists, evidenced by the increased number of patents describing MCH-1R antagonists for the treatment of obesity and metabolic syndrome. The structural diversity of small mol. weight drug-like MCH-1R antagonists produced and preclin. studies showing hypophagia and weight loss with small mol. weight and peptidal antagonists in rodents is encouraging and suggests that the identification of clin. candidates will be forthcoming.

REFERENCE COUNT: 97 THERE ARE 97 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:390227 CAPLUS
DOCUMENT NUMBER: 140:406742
TITLE: Preparation of ethynylpyridines and related compounds as melanin-concentrating hormone receptor (MCH-1) antagonist for the treatment of metabolic disorders.
INVENTOR(S): Mueller, Stephan-Georg; Stenkamp, Dirk; Arndt, Kirsten; Roth, Gerald Juergen; Lotz, Ralf Richard Hermann; Lehmann-Lintz, Thorsten; Lenter, Martin; Lustenberger, Philipp; Rudolf, Klaus
PATENT ASSIGNEE(S): Boehringer Ingelheim, Germany
SOURCE: PCT Int. Appl., 361 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039780	A1	20040513	WO 2003-EP11887	20031025
WO 2004039780	A8	20040715		
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DE 10250708	A1	20040519	DE 2002-10250708	20021031
CA 2504160	A1	20040513	CA 2003-2504160	20031025
AU 2003300507	A1	20040525	AU 2003-300507	20031025
EP 1558578	A1	20050803	EP 2003-809734	20031025
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BR 2003014839	A	20050830	BR 2003-14839	20031025
CN 1732154	A	20060208	CN 2003-80102635	20031025
JP 2006511492	T	20060406	JP 2004-547566	20031025
US 2004209865	A1	20041021	US 2003-697443	20031030
NO 2005000749	A	20050523	NO 2005-749	20050211

PRIORITY APPLN. INFO.:			
DE 2002-10250708	A	20021031	
US 2003-456543P	P	20030321	
WO 2003-EP11887	W	20031025	

OTHER SOURCE(S): MARPAT 140:406742
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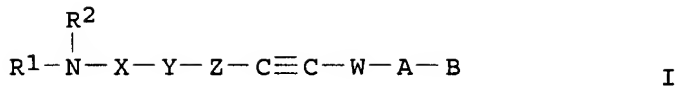

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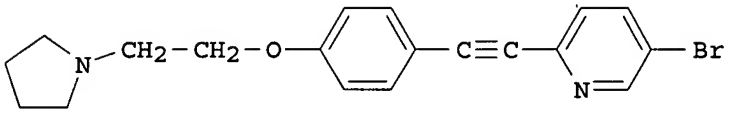

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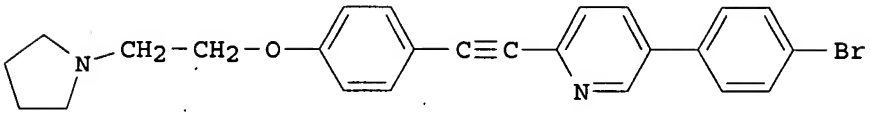

III

AB Title compds. I [R1, R2 = H, (un)substituted alkyl, cycloalkyl, etc; X = alkyl, alkenyl, alkynyl, etc.; W, Z = alkylene with provisos; Y = Cy with provisos; A = Cy; B = Cy, alkyl, alkenyl, etc.; Cy = (un)subsitiuted carbocycle, heterocycle] and their pharmaceutically acceptable salts and formulations were prepared For example, palladium mediated coupling of bromopyridine II, e.g., prepared from 4-iodophenol in 2-steps, and 4-bromophenylboronic acid afforded claimed ethynylpyridine III in 11% yield. In melanin concentrating hormone receptor (MCH-1R) binding assays, 2-examples of compds. I exhibited IC50 values ranging from 8-74 nM, e.g., the IC50 of ethynylpyridine III was 8 nM. Compds. I are claimed useful for the treatment of metabolic disorders and/or eating disorders, in particular, obesity, bulimia, anorexia, hyperphagia and diabetes.

L9 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:226656 CAPLUS

TITLE: Novel potent tetrazole containing Melanin Concentrating Hormone (MCH) receptor antagonists: Multi-component reactions lead the way

AUTHOR(S): Tempest, Paul A.; Nixey, Thomas; Ma, Vu; Balow, Guity; van Staden, Carlo; Salon, John; Rorer, Kirk; Baumgartner, Jamie; Hale, Clarence; Bannon, Tony; Hungate, Randall; Hulme, Christopher

CORPORATE SOURCE: Medicinal Chemistry Technologies, Chemistry Research & Development, Amgen, Thousand Oaks, CA, 91320, USA

SOURCE: Abstracts of Papers, 227th ACS National Meeting, Anaheim, CA, United States, March 28-April 1, 2004 (2004), MEDI-298. American Chemical Society: Washington, D. C.
CODEN: 69FGKM

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB Obesity has reached epidemic levels worldwide. Of patients who do lose weight, 95% regain all lost weight within 5 yr. Currently, 5 million patients are treated for obesity with an estimated 55 million going untreated in the US alone. Melanin Concentrating hormone (MCH) is a cyclic 19-amino acid neuropeptide that is an important regulator of energy balance in rodents. Evidence for its role as a modulator of energy balance include: 1) its location in brain areas associated with the control of feeding. 2) MCH levels are regulated in fasted and obese animals. 3) Intracerebroventricular administration increases food intake. 4) MCH knockout mice are lean and hypophagic. This poster reveals the one step library-derived discovery of novel highly potent, functionally active tetrazole based small mol. MCH1 receptor

antagonists. A rapid hit-lead transition and results from in vivo efficacy studies in fasted rats are also described.

L9 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:226655 CAPLUS
TITLE: Novel potent biaryl-ether containing Melanin Concentrating Hormone (MCH) receptor antagonists
AUTHOR(S): Ma, Vu; Tempest, Paul A.; van Staden, Carlo; Salon, John; Rorer, Kirk; Baumgartner, Jamie; Hale, Clarence; Bannon, Tony; Hulme, Christopher
CORPORATE SOURCE: Medicinal Chemistry Technologies, Chemistry Research & Development, Amgen, Thousand Oaks, CA, 91320, USA
SOURCE: Abstracts of Papers, 227th ACS National Meeting, Anaheim, CA, United States, March 28-April 1, 2004 (2004), MEDI-297. American Chemical Society: Washington, D. C.
CODEN: 69FGKM
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Obesity has reached epidemic levels worldwide. Of patients who do lose weight, 95% regain all lost weight within 5 yr. Currently, 5 million patients are treated for obesity with an estimated 55 million going untreated in the US alone. Melanin Concentrating hormone (MCH) is a cyclic 19-amino acid neuropeptide that is an important regulator of energy balance in rodents. Evidence for its role as a modulator of energy balance include: 1) its location in brain areas associated with the control of feeding. 2) MCH levels regulated in fasted and obese animals. 3) Intracerebroventricular administration increases food intake. 4) MCH knockout mice are lean and hypophagic. 5) MCH over-expressing mice have an obese phenotype. This poster reveals a library-derived discovery of a novel highly potent, functionally active, small mol. series of MCH1 receptor antagonists with the generic structure shown below 1. SAR studies and preliminary pharmacokinetic data are revealed.

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(FILE 'HOME' ENTERED AT 09:53:25 ON 14 MAR 2007)

FILE 'CAPLUS' ENTERED AT 09:53:56 ON 14 MAR 2007
L1 14 S MCH1 RECEPTOR ANTAGONIST?
L2 60 S MELANIN-CONCENTRATING HORMONE ANTAGONIST?
L3 3 S L1 AND DEPRESSION
L4 27 S L2 AND DEPRESSION
L5 30 S L3 OR L4
L6 2 S L1 AND ANXIETY
L7 21 S L2 AND ANXIETY
L8 23 S L6 OR L7
L9 8 S L1 AND OBESITY

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